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Manual Thrombus Aspiration and the Improved Survival of Patients With Unstable Angina Pectoris Treated With Percutaneous Coronary Intervention (30 Months Follow-Up)

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Abstract: The clinical effect of intracoronary thrombus aspiration during percutaneous coronary intervention in patients with unstable angina pectoris is unknown. In this study, we aimed to assess how thrombus aspiration during percutaneous coronary intervention affects in-hospital and 30-month mortality and complications in patients with unstable angina pectoris.

We undertook an observational cohort study of 645 consecutive unstable angina pectoris patients who had performed percutaneous coronary intervention from February 2011 to March 2013. Before intervention, 159 patients who had culprit lesion with thrombus were randomly assigned to group 1 (thrombus aspiration group) and group 2 (stand-alone percutaneous coronary intervention group). All patients were followed-up 30 months until August 2015.

Thrombus aspiration was performed in 64 patients (46%) whose cardiac markers (ie, creatinine kinase [CK-MB] mass and troponin T) were significantly lower after percutaneous coronary intervention than in those of group 2 (CK-MB mass: 3.80 ± 1.11 vs 4.23 ± 0.89 , $P = 0.012$; troponin T: 0.012 ± 0.014 vs 0.018 ± 0.008 , $P = 0.002$). Left ventricular ejection fraction at 6, 12, and 24 months postintervention was significantly higher in the group 1. During a mean follow-up period of 28.87 ± 6.28 months, mortality rates were 6.3% in the group 1 versus 12.9% in the group 2. Thrombus aspiration was also associated with significantly less long-term mortality in unstable angina pectoris patients (adjusted HR: 4.61, 95% CI: 1.16–18.21, $P = 0.029$).

Thrombus aspiration in the context of unstable angina pectoris is associated with a limited elevation in cardiac enzymes during intervention that minimises microembolization and significantly improves both of epicardial flow and myocardial perfusion, as shown by angiographic TIMI flow grade and frame count. Thrombus aspiration during percutaneous coronary intervention in unstable angina pectoris patients has better survival over a 30-month follow-up period.

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Abbreviations: ACS = acute coronary syndrome, CABG = coronary artery bypass grafting, CAD = coronary artery disease, CHF = congestive heart failure, CK-MB mass = creatinine kinase MB mass, CPM = cardiac pacemaker, CRT-D/P = cardiac resynchronization therapy and defibrillator/pacemaker, Cx = circumflex, DES = drug-eluting stent, GRACE = Global Registry of Acute Coronary Events, HF = heart failure, ICD = implantable cardioverter defibrillator, LAD = left anterior descending, LMCA = left main coronary artery, LV volume = left ventricular volume, LVEF = left ventricular ejection fraction, MBG = myocardial blush grade, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, QCA = quantitative coronary angiography, RCA = right coronary artery, REMEDIA = randomized evaluation of the effect of mechanical reduction of distal embolization by thrombus-aspiration in primary and rescue angioplasty, STEMI = ST-segment elevation myocardial infarction, TA = thrombus aspiration, TAPAS = Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study, TASTE = Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia, TFC = TIMI frame count, TIMI = thrombolysis in terms of myocardial infarction, UAP = unstable angina pectoris.

INTRODUCTION

Unstable angina pectoris (UAP) is the subset of acute coronary syndromes (ACS) caused by the erosion or rupture of atherosclerotic plaque and thrombosis.^{1,2} The prevalence of coronary thrombus has been estimated at 10% to 80% in patients with UAP.³ Primary therapy is often urgently needed and/or involves elective percutaneous coronary intervention (PCI).² During PCI, the percutaneous dilatation of coronary stenosis inevitably causes plaque disruption, which may in turn cause the distal embolization of plaque debris or thrombus material. Myocardial tissue reperfusion often reduces due to distal vascular debris embolization that prompts the plugging of the microvasculature, microvascular dysfunction, and myocardial necrosis.⁴

Recent studies using thrombectomy or a distal protection apparatus in primary PCI for ST segment elevation myocardial infarction (STEMI) have demonstrated that using such apparatuses can significantly reduce the incidence of distal embolization and improve both myocardial perfusion and clinical outcomes.^{5–9} Favorable outcomes have also been reported in patients with non-STEMI (NSTEMI) if angiography suggested the presence of thrombus formation.¹⁰ That study's analysis included PCI patients with UAP, in each of whom the application of manual aspiration catheter for thrombus aspiration (TA) during PCI was insufficient.¹¹ Currently, no published data comparing TA in patients with UAP are available. The primary aim of this observational study was to assess how TA

during PCI effects in-hospital and 30-month mortality in UAP patients. Its secondary aim was to assess this effect in relation to regional and global contractile left ventricular (LV) function, as well as examine how TA impacts on post-PCI thrombolysis in terms of myocardial infarction (TIMI) flow, TIMI frame count (TFC), and myocardial blush grade (MBG).

MATERIALS AND METHODS

Study Design and Population

The present research entailed a multicenter, retrospective, observational, cohort study involving the blind evaluation of end points confirmed by the local ethics committee and in accordance with the Declaration of Helsinki. We retrospectively studied 159 patients selected among 645 UAP patients consecutively referred to the catheterization laboratory of our institutions for coronary angiography and angioplasty. The analysis comprised PCI patients with UAP in each of whom the export aspiration catheter was applied for TA during PCI at Pamukkale University and Sifa University between February 15, 2011 and March 1, 2013. All patients were followed-up 30 months until August 1, 2015 except death.

UAP was defined as the occurrence of typical chest pain at rest with or without electrocardiographic signs of ischemia yet

without ST elevation or increase in cardiac troponin T greater than 0.01 ng/ml and creatinine kinase-MB (CK-MB) mass greater than 5 ng/ml (ie, local laboratory threshold of myocardial infarction). Inclusion criteria for UAP patients were thrombus burden vessel diameter greater than 2.5 mm, and technical viability for angioplasty independent of both initial TIMI flow and angiographic evidence of intraluminal thrombus in the culprit artery. Thrombus was defined as the presence of a roundish filling defect of the lumen during dye injection (in multiple projections either) with or without the persistence of luminal contrast following injection. Patients who had been taking anticoagulants and presented with cardiogenic shock and/or thrombus formation as a complication of a PCI (eg, vessel closure after stenting) were excluded from the sample. Other exclusion criteria were the known existence of a disease resulting in a life expectancy less than 6 months, and the lost of patient during follow-up. Patients with echocardiographic image of a poor quality were not accepted for the study. No other clinical exclusion criteria were adopted. The echocardiographic acoustic window was assessed in the emergency department or catheter laboratory by a staff cardiologist before the procedures. After enrollment and before PCI, 159 patients who had culprit lesion with thrombus were randomly assigned to group 1 (TA group) and group 2 (stand-alone PCI group) according to a computer-generated random series of numbers (Figure 1).

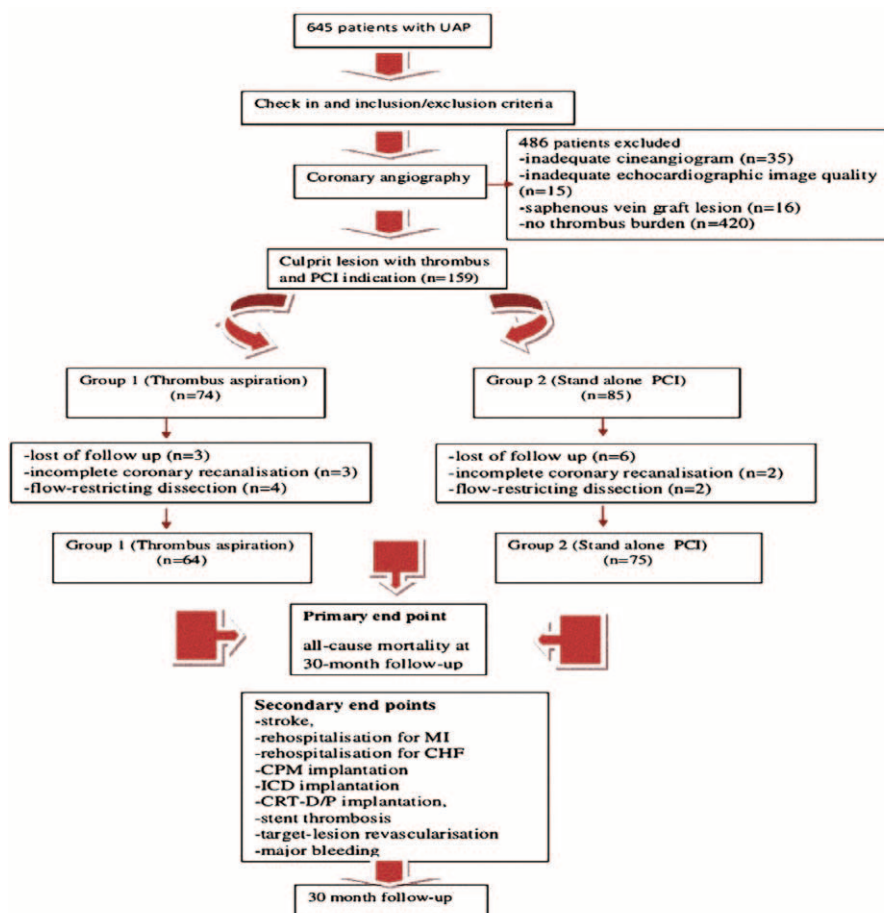


FIGURE 1. Flow diagram of the study profile.

Procedure

In all patients catheterization was performed following the femoral approach by experienced cardiologists. To begin, a steerable guide wire was passed through the target lesion; direct stenting was left to the operator's discretion and usually performed according to patent vessel with no or mild calcification. In patients in the group 2, this step was followed by balloon dilation to assure antegrade flow where as in those in the group 1, the step was followed by advancing the 6F export aspiration catheter (Medtronic, Minneapolis, MN), a 6F-compatible TA catheter with an aspiration lumen of 0.041 in. and cross profile of 0.068 in., which was handled over a guide wire of 0.014 in. in a monorail fashion. Suction was performed manually with lockable 20-ml syringes. After crossing the lesion with a guide wire, the export aspiration catheter was advanced into the target segment during continuous aspiration. The number of passages necessary to achieve an optimal result was left to the judgment of the operator, but at least 2×20 ml was aspirated in multiple passages. Additional balloon angioplasty was performed when necessary for stent delivery. After restoring the antegrade flow, in patients deemed suitable intracoronary nitrates were given to achieve maximal epicardial vasodilation, largely to determine the length, and size of the stent and facilitate stent placement.⁵ After placement, PCI postprocedural peak creatinine kinase MB mass (CK-MB) mass and troponin T level were measured. Measurement of CK-MB mass and troponin T were also repeated in 6, 24, and 48 h after PCI. Totally cardiac enzymes were measured 4 times after PCI.

Medication

Pharmacological treatment before and after PCI was performed according to European Society of Cardiology guideline.¹²

Angiographic and Echocardiographic Analysis

Coronary angiograms were performed digitally (INNOVA 2100, GE Healthcare, Waukesha, WI). Calibration of the quantitative coronary angiography (QCA) system was carried out by method in which the coronary catheter employed for angiography and was used as the calibration object by automated edge detection technique resulting in corresponding calibration factors (mm/pixel). The coronary artery contour was detected by operator independent edge detection algorithms. The dimension of the coronary artery was then measured as a function of catheter diameter; the absolute diameter in mm was calculated by the computerized software analysis. At least 2 orthogonal projections of the coronary segment scheduled for coronary intervention were filmed before and after the intervention. All angiograms were evaluated and reviewed offline by 2 experienced, interventional cardiologists blind both the results and success of the technique, as stated in the procedural report, for the presence of intraluminal filling defects and TIMI flow grade before PCI, after TA, and at the end of the procedure. The feasibility, success rate, and occurrence of potential complications (eg, coronary dissection and perforation) due to TA were reported. The applicability of the aspiration procedure was defined as the ability to advance the aspiration catheter into the target lesion without predilatation, while the accomplishment of TA was defined as the visually determined reduction of intraluminal filling defects in the angiogram and/or the presence of visible thrombus in the aspirate. Improvement in coronary flow due to TA was defined as the improvement in TIMI flow grade by at least one grade. Distal embolization during PCI was defined as the presence of a new distal occlusion of either the

treated vessel or one of its side branches or the migration of a filling defect. No reflow was defined as TIMI flow grade 0 to 1 not due to occlusive thrombus formation, dissection, or coronary artery spasm. Baseline, postaspiration, and final post-PCI angiographic coronary flows were also assessed by means of the corrected TFC at 12.5 frames/s.¹³ Baseline and final post-PCI MBGs were determined.¹⁴ Clinical status in terms of stroke, reinfarction, bleeding, pacemaker implantation, rehospitalization for heart failure (HF), target vessel revascularization, and death was determined from hospital records as well as by face to face interviews at 1, 6, 12, 24, and 30 months after the procedure.

LV ejection fraction (LVEF) and LV volumes were measured with the modified Simpson rule algorithm by echocardiography.¹⁵ The mean value of 3 measurements of the technically best cardiac cycles was taken from each examination. LVEF and LV volume changes at 6, 12, and 24 months were compared within 24 h of admission. Intraobserver and interobserver variability values in the evaluation of end-diastolic and -systolic volumes were $<5\%$, which suggests the good reproducibility of the measurements.¹⁶

Hospital Complications and Study End Points

In-hospital complications such as recurrent MI, stent thrombosis, atrial fibrillation, ventricular fibrillation, major bleeding (hemoglobin drop of 3–5 g% or need for blood transfusion, a drop in hemoglobin ≥ 5 g%, cardiac tamponade, need for surgical treatment or hemodynamic instability, and intracranial or intraocular bleeding), stroke, and acute renal failure were noted, in addition to 30-month mortality, complications, and major adverse cardiovascular events over a 30-month follow-up in patients undergoing PCI. The 30-month follow-up was 95% complete.

The primary end point was all-cause mortality at 30-month follow-up. We here report the following prespecified secondary end points: stroke, rehospitalization for MI and congestive heart failure (CHF), cardiac pacemaker (CPM), implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy and defibrillator/pacemaker (CRT-D/P) implantation, stent thrombosis, and target-lesion revascularization. The incidence of bleeding complications was assessed both during PCI and at 30 months following PCI.

Statistical Analysis

For quantitative variables, M and SD were calculated. Discrete variables are here presented as the number of events and their percentages. Comparisons were made with Chi-square or Fisher exact tests for discrete variables and by unpaired *t* tests, Wilcoxon sign-rank tests, or 1-way analyses of variance (ANOVA) for continuous variables. Repeated measured ANOVA was used for repeatedly measured variables. Survival curves were estimated using the Kaplan–Meier estimator and compared using log-rank tests while correlates of 30-month survival were determined using a multivariate backward stepwise Cox analysis. Cumulative hazard functions were computed to assess proportionality, and differences were considered significant at $P < 0.05$. Statistical analyses were performed by using the Statistical Package for the Social Sciences for Windows version 17 (SPSS, Chicago, IL).

RESULTS

Patient and Procedural Data

A total of 139 UAP patients (mean age 65.02 ± 13.00 years, 69.1% male) were studied, 64 of whom 46%

underwent thrombectomy. TA was attempted before PCI in UAP patients (aged 64.28 ± 12.7 years) who had angiography-detected of thrombus formation. Four hundred eighty-six patients were excluded from analysis (Figure 1). There were no statistically significant between-group differences in age, sex, duration of chest pain, risk factors (ie, body mass index, diabetes mellitus, hypertension, hyperlipidemia, smoking, renal insufficiency, family history and history of coronary artery disease [CAD], coronary artery bypass grafting [CABG], cerebrovascular accident, CHF, and peripheral artery disease), ECG parameters (ie, heart rate and rhythm at admission), blood parameters, drugs or medication taken before admission, LVEF within 24 h, Global Registry of Acute Coronary Events (GRACE) score, and Killip classification at admission. Baseline demographics and clinical characteristics are shown in Table 1.

The culprit coronary artery was the right coronary artery (RCA) in 34.4% of the group 1 and in 22.7% of the group 2, the left anterior descending artery (LAD) in 48.4% and 56% of the 2 groups, the left circumflex artery (Cx) in 15.6% and 18.7%, and the left main coronary artery (LMCA) in 1.6% and 2.7% ($P < 0.486$). Three and more vessel disease was present in 17.2% of patients in the group 1 versus 28% of patients in the group 2. Stent implantation was performed in 92.2% of patients in the group 1 and in 98.7% in the group 2. The use of a drug-eluting stent (DES) was similar in both groups ($P = 0.268$). Direct stenting was performed in 46 patients (34%). Cardiac markers (ie, CK-MB mass and troponin T) were significantly lower after PCI in the group 1 than the group 2 (CK-MB mass: 3.80 ± 1.11 vs 4.23 ± 0.89 , $P = 0.012$; troponin T: 0.012 ± 0.014 vs 0.018 ± 0.008 , $P = 0.002$). There were no statistically significant between-group differences in occlusion pre-PCI, balloon angioplasty, balloon length and diameter, balloon inflation time, inflator pressure, stent diameter and length, stent balloon inflation time, inflator pressure for stent balloon, stent postdilatation, or procedure complication (eg, coronary dissection, coronary perforation, hematoma, and arteriovenous fistula). Duration of hospitalization was statistically briefer in the group 1 than in the group 2 (4.25 ± 4.02 day vs 6.49 ± 5.83 day, $P = 0.011$). The use of anticoagulants and antiaggregants was generally similar between both groups, as was treatment by statins, β -blockers, ACEi, or ARB during the first 24 h. TA was associated with an increased rate of TIMI-flow 3 (37.5% in group 1 and 34.7% in the group 2 preprocedure vs 93.8% and 78.7%, respectively, at the end of procedure). The number of patients with postoperative TIMI grade 3 blood flow was significantly higher in the group 1 ($P = 0.036$). The number of patients with a no-reflow rate was lower in the group 1 than in the group 2, though not significantly ($P = 0.687$) while the incidence of MBG 3 was 90.6% and 70.3%, respectively ($P = 0.031$). TFCs were significantly decreased in infarct related arteries in both groups after PCI. The decrease in TFCs was far greater in the group 1 than in the group 2 and statistically significant (Table 2). Furthermore, a significant decrease in TFCs also emerged following aspiration in all coronary arteries in group 1 (TFC-LAD preaspiration: 25.93 ± 4.46 vs postaspiration: 17.25 ± 2.17 , $P = 0.001$; TFC-CX preaspiration: 20.07 ± 2.46 vs postaspiration: 14.35 ± 2.06 , $P = 0.001$; TFC-RCA preaspiration: 18.20 ± 5.33 vs postaspiration: 14.65 ± 2.59 , $P = 0.001$) (Table 3).

At 6, 12, and 24 months post-PCI, the mean LVEF was significantly higher in the group 1 versus the group 2 (Figure 2).

In-hospital mortality, stroke, stent thrombosis, major bleeding, recurrent MI, onset of atrial fibrillation (AF) or ventricular tachycardia/ventricular fibrillation (VT/VF), and

acute renal failure were not significantly different between the 2 groups (Table 4).

Death, stroke, bleeding complications, recurrent MI, stent thrombosis, occurrence of AF, occurrence of VT/VF, new renal dialysis, new CABG, rehospitalization for HF, CPM implantation, ICD or CRT-D/P implantation were assessed within 30 months following PCI. Death was significantly lower in the group 1 (unadjusted OR: 0.29, 95% CI: 0.09–0.93, $P = 0.030$). In a multiple logistic regression model adjusted for age, sex, systolic blood pressure, glomerular filtration rate, multivessel CAD, GRACE score at admission, initial TIMI flow, LVEF at 6 months, or concomitant use of GP IIb–IIIa inhibitors, TA was associated with a significant reduction in 30-month mortality (adjusted OR: 7.36, 95% CI: 1.20–45.10, $P = 0.031$). Stroke, recurrent MI, occurrence of AF, occurrence of VT/VF, ICD implantation, rehospitalization for HF, new CABG were also significantly lower in the group 1 than in the group 2 (Table 5).

During a mean follow-up period of 28.87 ± 6.28 months (30.18 ± 4.16 months in the group 1 vs 27.76 ± 7.49 months in the group 2), 18 patients (12.9%) died. Of these, 4 patients were from the group 1 (6.3%) and 14 from the group 2 (18.7%) (unadjusted HR: 3.24, 95% CI: 1.06–9.58, $P = 0.038$). Using Cox multivariate analysis, TA was associated with significantly less long-term mortality even after the same variables were corrected in all UAP patients (adjusted HR: 4.61, 95% CI: 1.16–18.21, $P = 0.029$). The Kaplan–Meier cumulative survive curve appears in Figure 3.

DISCUSSION

In this trial, the process of manual TA during PCI in patients with UAP and thrombus-containing lesions was found to be associated with better long-term survival and lower rates of stroke, recurrent MI, arrhythmias (AF, VT/VF), rehospitalization for CHF, and new CABG and ICD implantation within 30 months than in patients treated with PCI only. To the best of our knowledge, this study is the first of PCI-treated UAP patients to have demonstrated an association between TA and reduced mortality.

Previous studies assessing the use of TA in STEMI patients and its outcomes have demonstrated different results.^{5,8,17–20} The Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study (TAPAS) is the only randomized trial to have demonstrated a significant beneficial effect on mortality: an approximately 50% reduction in 1-year mortality.⁸ Conversely, the Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE) study showed that routine thrombectomy use did not reduce 30-day mortality.²¹ Similar conflicting results were demonstrated in NSTEMI patients. Vlaar et al¹⁰ found that manual TA was associated with a significant reduction of TIMI thrombus score and an increased rate of TIMI flow grade 3 in NSTEMI patients. Thiele et al²² showed that TA in conjunction with PCI in NSTEMI with a thrombus-containing lesion did not precipitate any reduction in microvascular obstruction. Hermens et al¹¹ published their initial experiences with manual TA in 14 patients with stable or UAP and recommended that myocardial perfusion might benefit from TA in patients with stable or unstable angina. Based on these data, current American and European guidelines suggest performing manual TA in only STEMI patients with a class IIa level of evidence B recommendation.^{23,24}

In this study, manual TA was associated with a significant reduction of TFC and an increase in the rate of TIMI flow 3 and

TABLE 1. Baseline Characteristics of Study Population

	Thrombus Aspiration			Stand-Alone PCI			P
	(n)	Mean ± SD	(%)	(n)	Mean ± SD	(%)	
Age (y)		64.28 ± 12.70			65.65 ± 13.30		0.537
Duration of chest pain (h)		6.85 ± 3.62			7.07 ± 4.32		0.755
Sex							0.941
Female	20		31.3	23		30.7	
Male	44		68.8	52		69.3	
Risk factors							
BMI (kg/m ²)		26.00 ± 2.30			26.08 ± 2.51		0.846
DM	24		37.5	25		33.3	0.608
HT	39		60.9	40		53.3	0.367
HLP	13		20.3	19		25.3	0.483
Smoking	19		29.7	25		33.3	0.645
Family history	10		15.6	11		14.7	0.875
History							
Previous CAD	12		18.8	17		22.7	0.571
Previous PAD	5		7.8	6		8.0	0.967
Previous CABG	7		10.9	8		10.7	0.959
Previous CVA	3		4.7	5		6.7	0.726*
Previous CHF	5		7.8	4		5.3	0.732*
Chronic renal failure	9		14.1	15		20.0	0.356
Clinical							
SBP (mm Hg)		143.73 ± 11.83			142.45 ± 16.49		0.605
DBP (mm Hg)		85.39 ± 14.06			83.98 ± 17.53		0.608
ECG							
HR beats/min		78.14 ± 19.24			75.61 ± 16.54		0.406
Rhythm at admission							0.754
SR	57		89.1	68		90.7	
AF	7		10.9	7		9.3	
RBBB	7		10.7	6		8.0	0.553
LBBB	12		18.8	11		14.7	0.518
AV block	11		17.2	20		26.7	0.181
Bloods							
Hg (g/dl)		13.01 ± 2.37			13.34 ± 1.78		0.354
Plt (k/μl)		232.10 ± 41.52			220.44 ± 51.50		0.148
WBC (k/μl)		7.74 ± 1.55			7.50 ± 1.30		0.328
Urea (mg/dl)		37.09 ± 14.26			42.32 ± 22.25		0.108
Creatinine (mg/dl)		1.01 ± 0.27			1.01 ± 0.29		0.978
GFR (ccs/min)		83.71 ± 33.54			76.25 ± 31.75		0.181
Hs-CRP (mg/L)		2.79 ± 1.20			2.59 ± 0.93		0.272
Uric acid (mg/dl)		7.03 ± 2.18			7.21 ± 1.86		0.615
Glucose (mg/dl)		132.35 ± 36.98			134.40 ± 69.32		0.833
CK-MB mass (ng/ml) [†]		2.39 ± 0.97			2.26 ± 1.06		0.456
Troponin T (ng/ml) [‡]		0.0034 ± 0.0038			0.0034 ± 0.0040		0.910
LDL cholesterol (mg/dl)		112.34 ± 31.99			109.02 ± 28.07		0.516
HDL cholesterol (mg/dl)		42.62 ± 9.43			40.68 ± 11.28		0.277
Triglyceride (mg/dl)		208.14 ± 86.71			197.28 ± 109.62		0.523
Total cholesterol (mg/dl)		192.70 ± 26.44			195.90 ± 32.64		0.531
Drugs before admission							
Aspirin	22		34.4	34		45.3	0.189
Clopidogrel	13		20.3	14		18.7	0.807
ACEi or ARB	34		53.1	42		56.0	0.734
β-blocker	36		56.3	36		48.0	0.332
Statin	17		26.6	26		34.7	0.303
LVEF%							
Within 24 h		47.26 ± 9.87			46.21 ± 9.94		0.534
GRACE score (death)		93.62 ± 24.79			100.40 ± 18.33		0.067
GRACE score (death + MI)		114.40 ± 28.69			122.86 ± 22.74		0.055
Admission Killip class		1.34 ± 0.47			1.32 ± .52		0.782

ACEi = angiotensin converting enzyme inhibitor, AF = atrial fibrillation, ARB = angiotensin receptor blocker, AV block = atrioventricular block, BMI = body mass index, CABG = coronary artery bypass grafting, CAD = coronary artery disease, CHF = congestive heart failure, CK-MB mass = creatinine kinase MB mass, CVA = cerebrovascular accident, DBP = diastolic blood pressure, DM = diabetes mellitus, GFR = glomerular filtration rate, HDL = high density lipoprotein, Hg = hemoglobin, HLP = hyperlipidemia, HR = heart rate, HT = hypertension, LBBB = left bundle branch block, LDL = low density lipoprotein, LVEF = left ventricular ejection fraction, NSTEMI = non-ST-segment elevation myocardial infarction, PAD = peripheral artery disease, PCI = percutaneous coronary intervention, Plt = platelet, RBBB = right bundle branch block, SBP = systolic blood pressure, SD = standard deviation, SR = sinus rhythm, STEMI = ST-segment elevation myocardial infarction, UAP = unstable angina pectoris, VT = ventricular tachycardia, WBC = white blood cell.

* Fischer exact test was used.

[†] CK-MB mass normal range: 0–5 ng/ml.

[‡] Troponin T normal range: 0–0.014 ng/ml.

TABLE 2. Procedural Characteristics, Angiographic, and Echocardiographic Results of Study Population

	Thrombus Aspiration			Stand-Alone PCI			<i>P</i>
	(n)	Mean ± SD	(%)	(n)	Mean ± SD	(%)	
Culprit coronary vessel							0.486
LMCA	1		1.6	2		2.7	
CX	10		15.6	14		18.7	
LAD	31		48.4	42		56	
RCA	22		34.4	17		22.7	
CAD extension							0.036
1 vessel	37		57.8	27		36.0	
2 vessels	16		25.0	27		36.0	
3 and more vessels	11		17.2	21		28.0	
Balloon angioplasty	51		79.7	53		70.7	0.222
Stent implanted	61		95.3	74		98.7	0.334*
Stent type							0.684
BMS	22		34.4	30		40.0	
DES	39		60.9	43		57.3	
Direct stenting	19		29.7	27		36.0	0.476
Occlusion pre-PCI (%)		92.17 ± 4.46			90.71 ± 6.32		0.212
Balloon diameter (mm)		1.81 ± 1.13			1.67 ± 1.26		0.500
Balloon length (mm)		13.72 ± 8.19			12.52 ± 9.91		0.444
Balloon inflation time (s)		27.58 ± 18.12			27.60 ± 22.27		0.995
Indeflator pressure (atm)		10.34 ± 5.62			9.45 ± 7.08		0.419
Stent diameter (mm)		2.80 ± 0.82			2.84 ± 0.61		0.773
Stent length (mm)		20.89 ± 8.58			21.69 ± 10.89		0.634
Stent balloon inflation time (s)		20.47 ± 9.98			19.07 ± 7.38		0.344
Indeflator pressure for stent balloon (atm)		14.70 ± 3.80			14.64 ± 3.03		0.920
Stent postdilatation	7		10.9	7		9.3	0.754
No-reflow	2		3.1	4		5.3	0.687*
Procedure complication	10		15.6	10		13.3	0.701
Procedure complication type							0.572
Coronary dissection	4		40.0	2		20.0	
Coronary perforation	0		0	1		10.0	
Hematoma	5		50.0	5		50.0	
Arteriovenous fistula	1		10.0	2		20.0	
Post-PCI CK-MB mass (ng/ml)		3.80 ± 1.11			4.23 ± 0.89		0.012
Post-PCI troponin T (ng/ml)		0.012 ± 0.014			0.018 ± 0.008		0.002
Hospitalization time (d)		4.25 ± 4.02			6.49 ± 5.83		0.011
Drugs							
Glycerol trinitrate (before/during angiography)	16		25.0	23		30.7	0.459
Glycoprotein IIb–IIIa inhibitors (before/during angiography)	12		18.8	8		10.7	0.176
Ca-channel blocker (before/during angiography)	8		12.5	8		10.7	0.736
Aspirin in first 24 h	62		96.9	73		97.3	0.872
Clopidogrel first	49		76.6	55		73.3	0.662
Prasugrel first	5		7.8	6		8.0	0.967
LMWH (before/during angiography)	49		76.6	47		62.7	0.077
UFH (before/during angiography)	31		48.4	46		61.3	0.127
Statin in first 24 h	39		60.9	52		69.3	0.299
ACEi or ARB in first 24 h	30		46.9	33		44.0	0.734
β blockers in first 24 h	29		45.3	37		49.3	0.636
TIMI flow before PCI							0.718
1	9		14.1	8		10.7	
2	31		48.4	41		54.7	
3	24		37.5	26		34.7	
TIMI flow after PCI							0.036
1	1		1.6	2		2.7	
2	3		4.7	14		18.7	
3	60		93.8	59		78.7	
Myocardial blush grade pre-PCI							0.553

TABLE 2. (Continued)

	Thrombus Aspiration			Stand-Alone PCI			P
	(n)	Mean ± SD	(%)	(n)	Mean ± SD	(%)	
1	10		15.6	8		10.7	
2	34		53.1	46		61.3	
3	20		31.3	21		28	
Myocardial blush grade post-PCI							0.031
1	1		1.6	2		2.7	
2	5		7.8	18		24.0	
3	58		90.6	55		73.3	
TIMI frame count							
LAD							
Pre-PCI	31	25.93 ± 4.46		42	24.01 ± 2.76		0.050
Post-PCI	31	15.43 ± 3.07		42	18.18 ± 1.39		0.001
Cx							
Pre-PCI	10	21.00 ± 3.65		14	20.07 ± 2.46		0.438
Post-PCI	10	13.78 ± 2.69		14	16.78 ± 2.11		0.003
RCA							
Pre-PCI	22	18.20 ± 5.33		17	18.62 ± 3.30		0.779
Post-PCI	22	14.13 ± 2.48		17	16.12 ± 3.00		0.027
EF%							
After 6 months post-PCI	63	53.12 ± 8.57		73	49.54 ± 10.12		0.029
After 12 months post-PCI	63	52.38 ± 10.62		70	48.18 ± 12.19		0.037
After 24 months post-PCI	62	52.54 ± 11.39		61	48.03 ± 11.86		0.033

ACEi = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, BMS = bare metal stent, CAD = coronary artery disease, Cx = circumflex, CK-MB mass = creatinine kinase MB mass, DES = drug eluting stent, LAD = left anterior descending, LMCA = left main coronary artery, LMWH = low molecular weight heparin, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, RCA = right coronary artery, SD = standard deviation, STEMI = ST-segment elevation myocardial infarction, TIMI = thrombolysis in myocardial infarction, UAP = unstable angina pectoris, UFH = unfractionated heparin.

Bold value signifies statistically significant.

* Fischer exact test was used.

MBG 3 in the manual TA group. Vlaar et al¹⁰ found an increase in TIMI 3 flow after TA in NSTEMI patients while Burzotta et al¹⁷ found significant improvement of MBG in patients with successful TA in STEMI patients. In our study, postprocedural levels of CK-MB mass and troponin T were higher in the stand-alone PCI group than in the TA group. These results show

that TA reduces thrombus burden and prevents distal embolization in causing microvascular injury. Thereby, increased microvascular flow improves myocardial reperfusion and clinical outcomes.^{25,26}

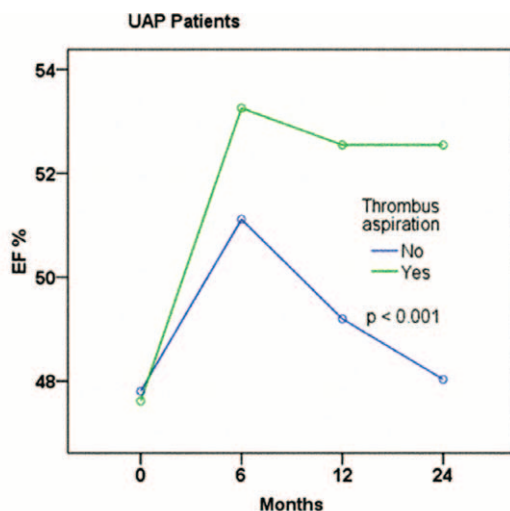
In the present study, we also evaluated LV functions of UAP patients, and baseline LVEFs were similar between the 2

TABLE 3. Comparison of TIMI Frame Counts of All Patients

Thrombus Aspiration (+)	TIMI Frame Count					
	Pre-Asp	Post-Asp	Post-PCI	P, Pre-Asp–Post-Asp	P, Pre-Asp–Post-PCI	P, Post-Asp–Post-PCI
LAD (n = 31)	25.93 ± 4.46	17.25 ± 2.17	15.43 ± 3.07	0.001	0.001	0.028
CX (n = 10)	20.07 ± 2.46	14.35 ± 2.06	13.78 ± 2.69	0.001	0.001	0.120
RCA (n = 22)	18.20 ± 5.33	14.65 ± 2.59	14.13 ± 2.48	0.001	0.001	0.037
Thrombus Aspiration (–)	TIMI Frame Count					
	Pre-PCI	Post-PCI	P, Pre-PCI–Post-PCI			
LAD (n = 42)	24.01 ± 2.74	18.18 ± 1.39	0.001			
CX (n = 14)	21.00 ± 3.65	16.78 ± 2.11	0.001			
RCA (n = 17)	18.62 ± 3.30	16.12 ± 3.00	0.001			

Cx = circumflex, LAD = left anterior descending, PCI = percutaneous coronary intervention, Post-asp = postthrombus aspiration, Pre-asp = prethrombus aspiration, RCA = right coronary artery, TIMI = thrombolysis in terms of myocardial infarction.

Bold value signifies $P < 0.05$.



Stand alone PCI (n)	75	73	70	61
Thrombus aspiration (n)	64	63	63	62

FIGURE 2. Two-year LVEF according to the use of thrombus aspiration in UAP patients. *P* values come from repeated measured analysis of variance.

groups. By the time that LVEFs were changed in 6, 12, and 24 months after PCI in both groups. LVEF was significantly higher in the TA group than in the stand-alone group during 24 months. The LVEF increases in both groups at the 1st echo during follow-up, then goes down and plateaus in the thrombectomy group while declining further in the nonthrombectomy group. We may accept that LVEF is acutely depressed or biomarker release (hibernation) and that it improves after revascularization. Decrease in LVEF in the stand-alone PCI group after 6 months may be explained by higher incidence of complications like recurrent MI in this group. Similarly, Liistro et al²⁷ showed that manual TA in the context of primary PCI improves myocardial tissue-level perfusion as well as LV functional recovery and remodeling at 6 months. Conversely, in the myocardial contrast echocardiographical substudy of the REMEDIA trial,²⁸ TA was associated with no significant reduction in LV remodeling at 6 months. Despite conflicting results, our findings suggest that TA may help to reduce the infarct size and preserve the myocardial function by protecting microvascular obstruction.

According to our study, TA appears to be a valuable approach to improving outcomes in UAP patients with visible thrombus. In this study, improved procedural outcomes with manual TA were observed, though these improvements were not associated with better hospital mortality or in-hospital complication rates. Although there was no significant difference in relationship to hospital complications, duration of hospitalization was significantly briefer in the TA group. Lower long-term complication rates may be attributed to the use of TA during PCI, since TA may help to reduce infarct size, prevent cardiac remodeling, and/or preserve myocardial function by

TABLE 4. In-Hospital Complications

	Thrombus Aspiration Group	Stand-Alone PCI Group	<i>P</i> , Odds Ratio (95% CI)
Death			1.000*
(n)	1	2	0.579
(%)	1.6	2.7	(0.051–6.542)
Stroke			0.624*
(n)	1	3	0.381
(%)	1.6	4	(0.039–3.755)
Stent thrombosis			0.452*
(n)	2	5	0.452
(%)	3.1	6.7	(0.085–2.411)
Major bleeding			0.993
(n)	6	7	1.005
(%)	9.4	9.3	(0.320–3.159)
Recurrent MI			0.624*
(n)	1	3	0.381
(%)	1.6	4	(0.039–3.755)
Onset AF			0.343
(n)	6	11	0.602
(%)	9.4	14.7	(0.209–1.731)
Onset VT/VF			0.086
(n)	2	8	0.270
(%)	3.1	10.7	(0.055–1.322)
Acute renal failure			0.291
(n)	3	7	0.478
(%)	4.7	9.3	(0.118–1.930)

AF = atrial fibrillation, CI = confidence interval, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction, UAP = unstable angina pectoris, VT/VF = ventricular tachycardia, ventricular fibrillation.

*Fischer exact test was used.

TABLE 5. Comparison of Complications Over 30 Months Following in Patients Undergoing Percutaneous Coronary Intervention (PCI)

	Thrombectomy Group	Stand-Alone PCI Group	P, Odds Ratio (95% CI)
Death			0.030
(n)	4	14	0.290
(%)	6.3	18.7	(0.090–0.933)
Stroke			0.033
(n)	2	10	0.210
(%)	3.1	13.3	(0.044–0.995)
Stent thrombosis			0.246
(n)	4	9	0.489
(%)	6.3	12	(0.143–1.670)
Major bleeding			0.901
(n)	9	10	1.064
(%)	14.1	13.3	(0.403–2.804)
Recurrent MI			0.030
(n)	4	14	0.290
(%)	6.3	18.7	(0.090–0.933)
AF			0.032
(n)	3	12	0.258
(%)	4.7	16	(0.069–0.960)
VT/VF			0.019
(n)	4	15	0.267
(%)	6.3	20	(0.084–0.850)
ICD implantation			0.027
(n)	5	16	0.313
(%)	7.8	21.3	(0.108–0.908)
CRT-D/P implantation			0.506*
(n)	3	6	0.566
(%)	4.7	8	(0.136–2.359)
CPM implantation			1.000*
(n)	2	2	1.177
(%)	3.1	2.7	(0.161–8.605)
Rehospitalization for HF			0.015
(n)	6	19	0.305
(%)	9.4	25.3	(0.113–0.819)
New renal dialysis			0.051
(n)	3	11	0.286
(%)	4.7	14.7	(0.076–1.075)
New CABG			0.030
(n)	4	14	0.290
(%)	6.3	18.7	(0.090–0.933)

AF=atrial fibrillation, CABG=coronary artery bypass grafting, CI=confidence interval, CPM=cardiac pacemaker, CRT-D/P=cardiac resynchronization therapy and defibrillator/pacemaker, HF=heart failure, ICD=implantable cardioverter defibrillator, NSTEMI=non-ST-segment elevation myocardial infarction, STEMI=ST-segment elevation myocardial infarction, UAP=unstable angina pectoris, VT/VF=ventricular tachycardia/ventricular fibrillation.

* Fischer exact test was used.

protecting microvascular obstruction. Lower stroke rates up until the 30-month follow-up in our study can be explained by a significant reduction in the onset of AF or VT/VF.

Study Limitations

In this study, for UAP patients the decision to perform TA was made after careful consideration by experienced interventional cardiologists. Nevertheless, absent the use of intravascular ultrasound or optical coherence tomography, even experienced operators have a limited ability to distinguish intracoronary thrombus formation from calcified lesions. Our data lack information on culprit lesion characteristics (eg,

target-vessel tortuosity). In addition, we have not standardized our determination of whether the aspiration catheter crossed the culprit lesion and lacked information concerning the amount of thrombus material removed. Also, the study population remained small.

CONCLUSIONS

This study demonstrates that manual TA in the context of UAP is associated with a limited elevation in cardiac enzymes during PCI that minimizes microembolization with a significant improvement both of the coronary artery flow and myocardial perfusion, as assessed by the use angiographic TIMI flow grade, TFC, and MBG. The improvement in tissue perfusion is also

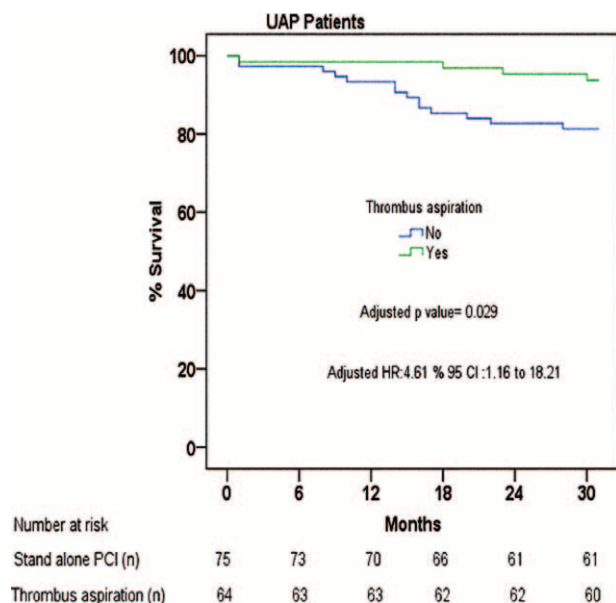


FIGURE 3. Kaplan–Meier curves for overall survival up to 30-month follow-up according to the use of thrombus aspiration in UAP patients. Log-rank: χ^2 : 4.83, $P < 0.028$.

associated with a significant improvement in regional and global LV function at 24 months. Our findings further support the use of thrombectomy during PCI in UAP patients given its association with better survival over a 30-month follow-up period. Using thrombectomy given the suspicion of thrombus formation in UAP patients affords better results. Nevertheless, further studies with larger sample sizes are needed to evaluate the clinical value of and long-term prognosis following this procedure.

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